Infectious Disease Models 1

Nathaniel Osgood

CMPT 858

March 9, 2010

Comments on Mathematics & Dynamic Modeling

- Many accomplished & well-published dynamic modelers have very limited mathematical background
  - Can investigate pressing & important issues
  - Software tools are making this easier over time
- Can gain extra insight/flexibility if willing to push to learn some of the associated mathematics
- Achieving highest skill levels in dynamic modeling do require mathematical facility and sophistication
  - To do sophisticated work, often those lacking this background or inclination collaborate with someone with background

Applied Math & Dynamic Modeling

- Although you may not use it, the dynamic modeling presented rests on the tremendous deep & rich foundation of applied mathematics
  - Linear algebra
  - Calculus (Differentia/Integral, Uni& Multivariate)
  - Differential equations
  - Numerical analysis (including numerical integration, parameter estimation)
  - Control theory
  - Real & complex analysis
- For the mathematically inclined, the tools of these areas of applied math are available

Models in Mathematical Epidemiology of Infectious Disease

- Long & influential modeling tradition, beginning with Kermack-McKendrick (1920s)
- Models formulated for diverse situations (Cf. Anderson & May)
  - Latent & incubation period/Diversity in contact rates/Heterogeneity/Preferential mixing/Vaccinated groups/Zoonoses/Variations in clinical manifestations/Network structure
- Important tradition of closed-form analysis

Mathematical Models Link Together Diverse Factors

Typical Factors Included

- Infection
  - Mixing & Transmission
  - Development & loss of immunity – both individual and collective
  - Natural history (often multi-stage progression)
  - Recovery
- Birth & Migration
- Aging & Mortality
- Intervention impact

Sometimes Included

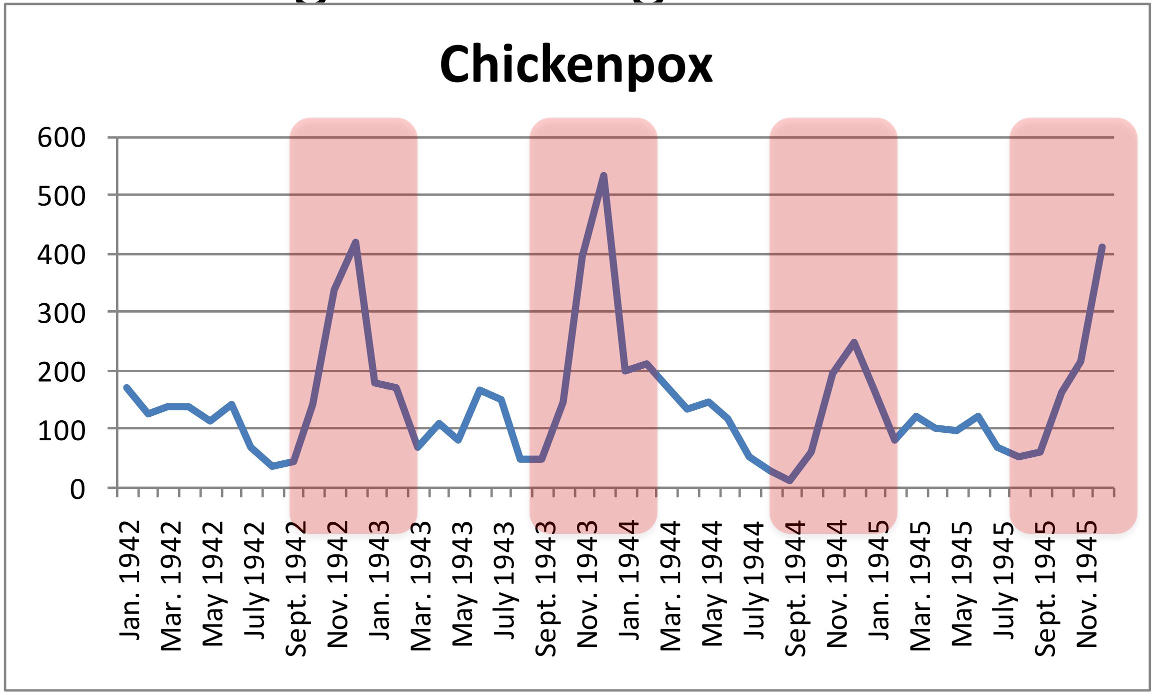
- Preferential mixing
- Variability in contacts
- Strain competition & cross-immunity
- Quality of life change
- Health services interaction
- Local perception
- Changes in behavior, attitude
- Immune response

Emergent Characteristics of Infectious Diseases Models

- Instability
- Nonlinearity
- Tipping points
- Oscillations
- Multiple fixed points/equilibria
  - “Endemic” equilibrium
  - Disease free equilibrium

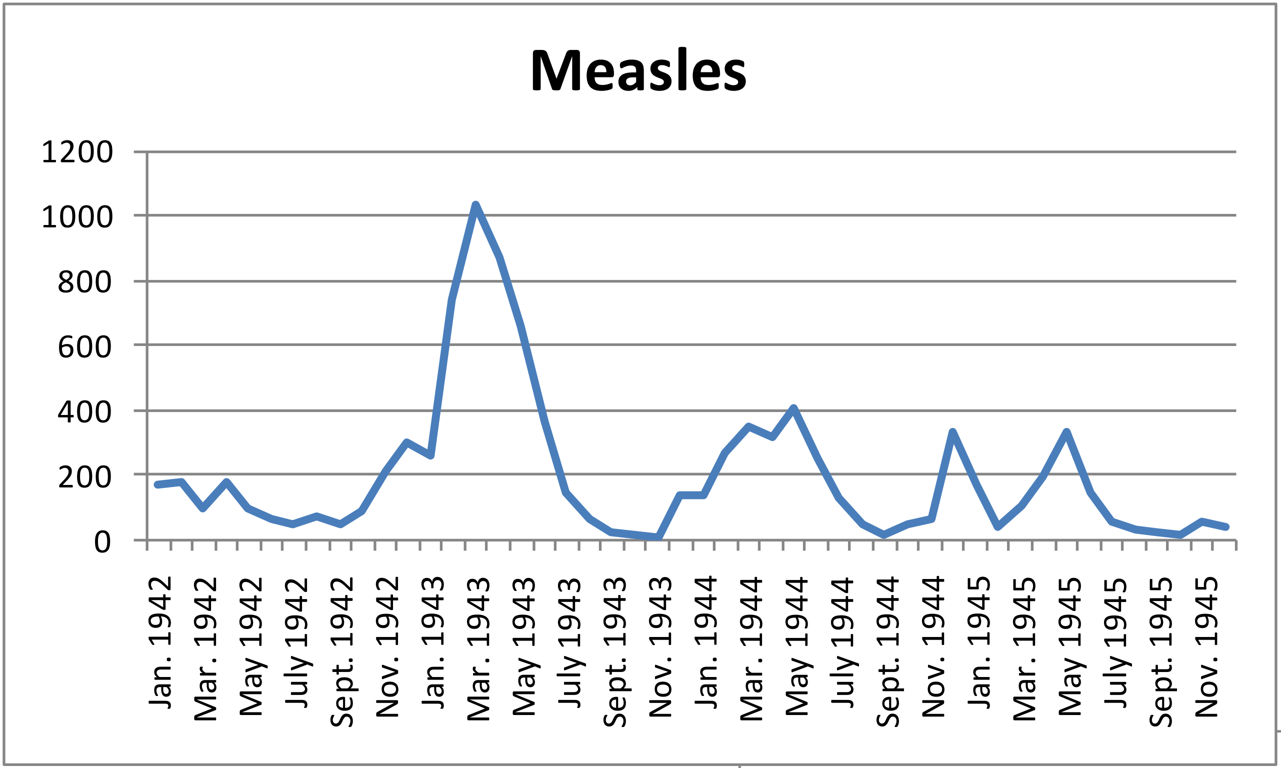
Instability

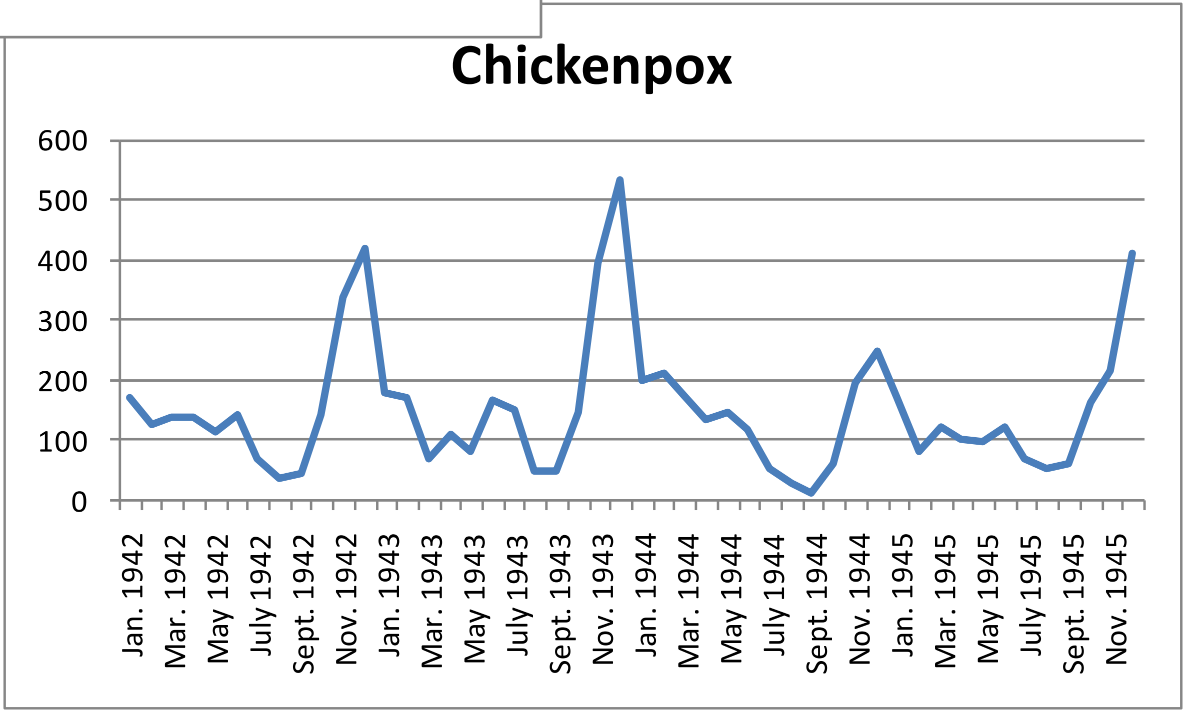
- Slight perturbation (e.g. arrival of infectious person on a plane) can cause big change in results
  - Contrast with "goal seeking" behaviour



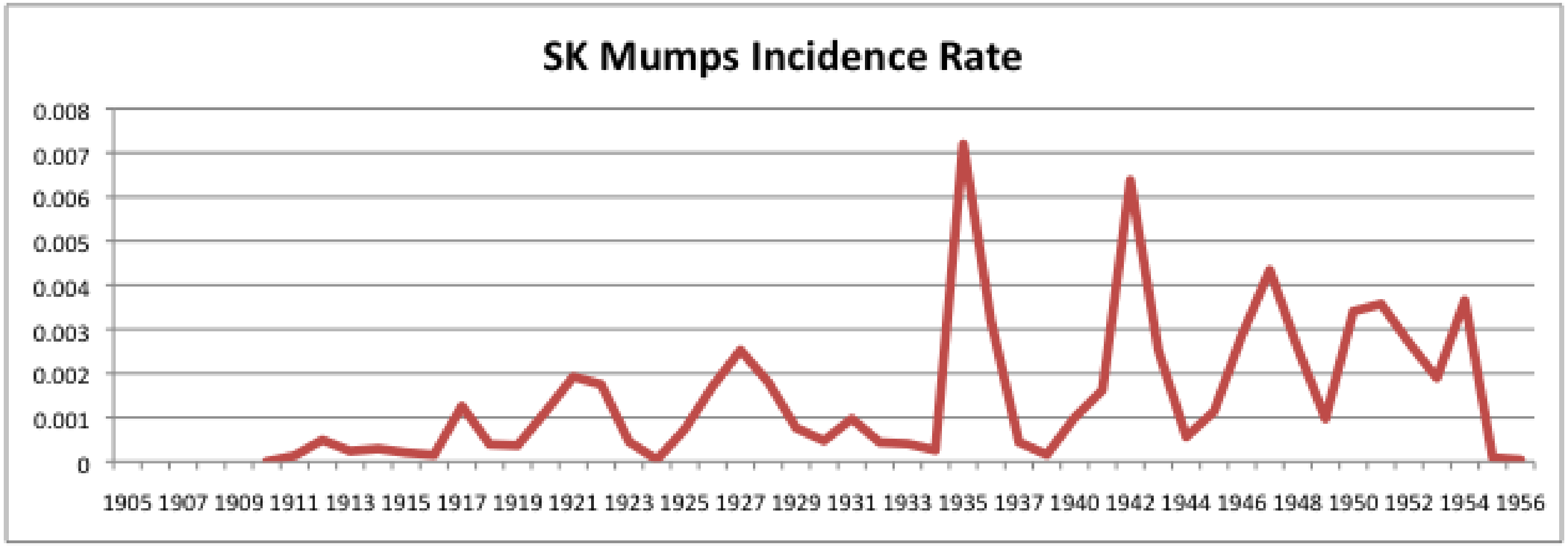
Oscillations & Delays

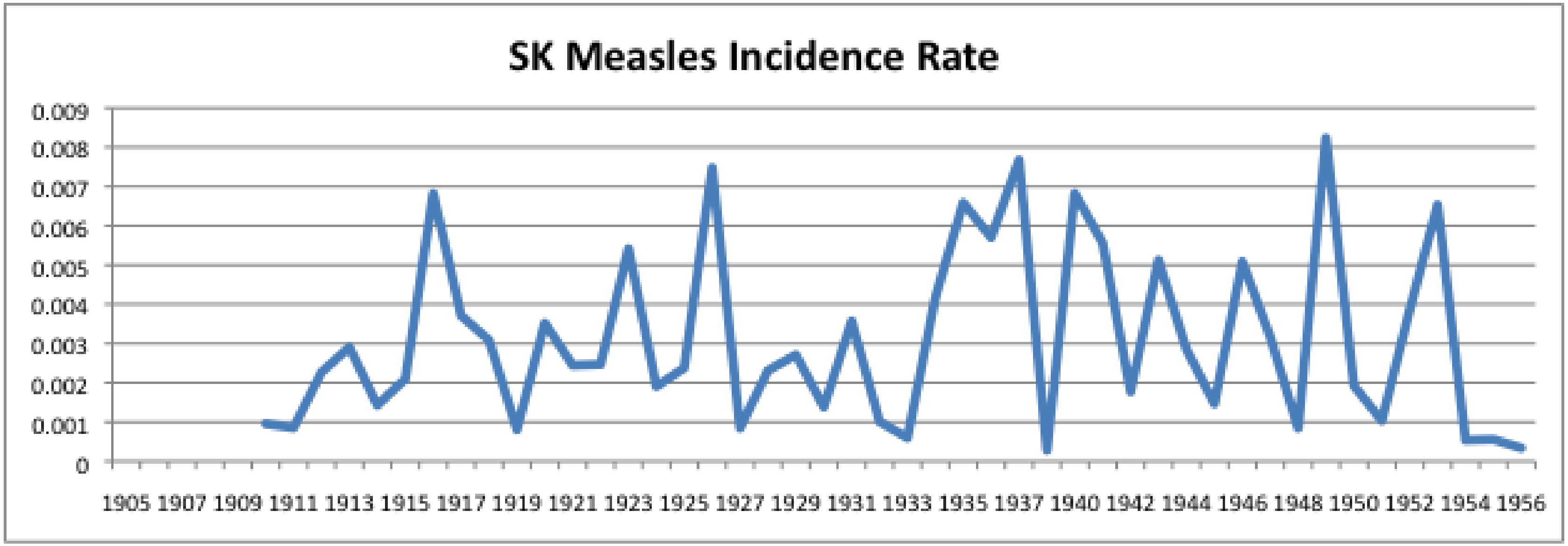
- The oscillations reflect negative feedback loops with delays
- These delays reflect “stock and flow” considerations and specific thresholds dictating whether net flow is positive or negative
  - Stock & Flow: Stock continues to deplete as long as outflow exceeds inflow, rise as inflow>outflow
    - The stock may stay reasonably high long after inflow is low!
  - Key threshold R*: When # of individuals being infected by a single infective = 1
    - This is the threshold at which outflows=inflows

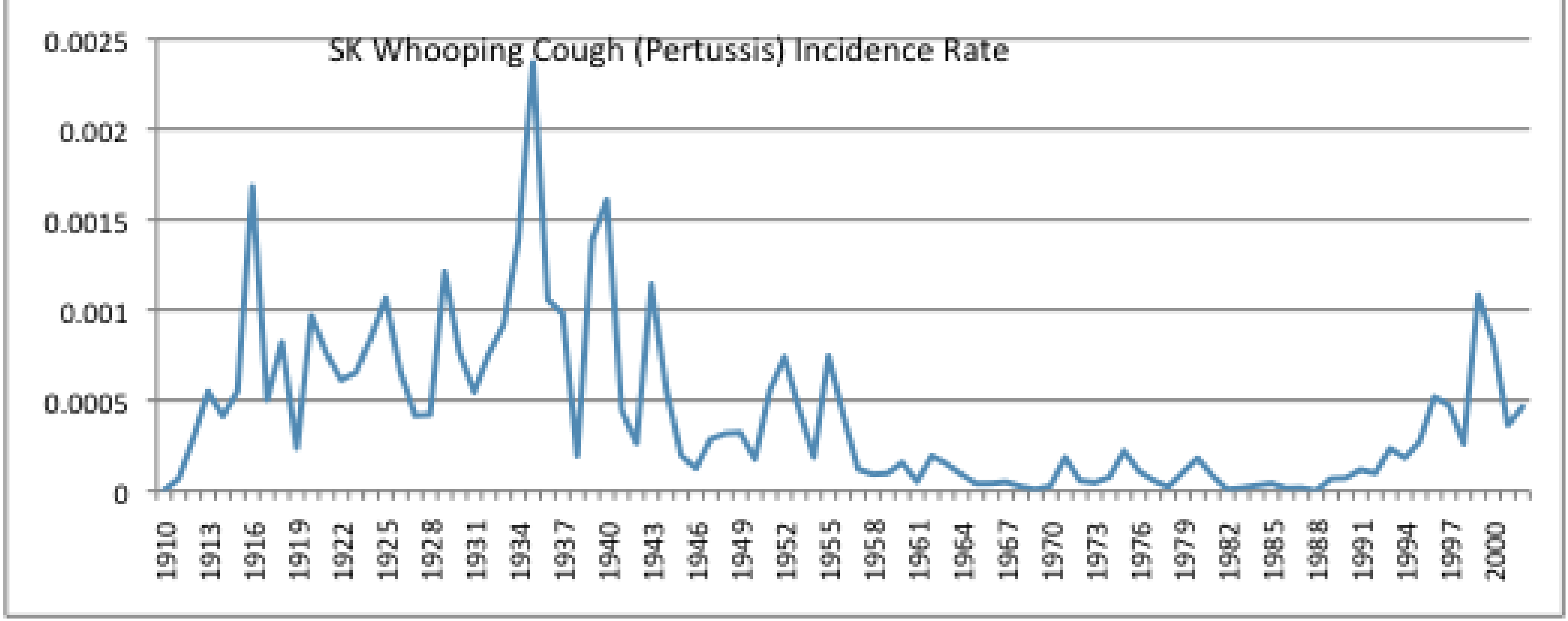

Measles
1200
1000
800
600
400
200
0
Jan. 1942
Mar. 1942
May 1942
July 1942
Sept. 1942
Nov. 1942
Jan. 1943
Mar. 1943
May 1943
July 1943
Sept. 1943
Nov. 1943
Jan. 1944
Mar. 1944
May 1944
July 1944
Sept. 1944
Nov. 1944
Jan. 1945
Mar. 1945
May 1945
July 1945
Sept. 1945
Nov. 1945

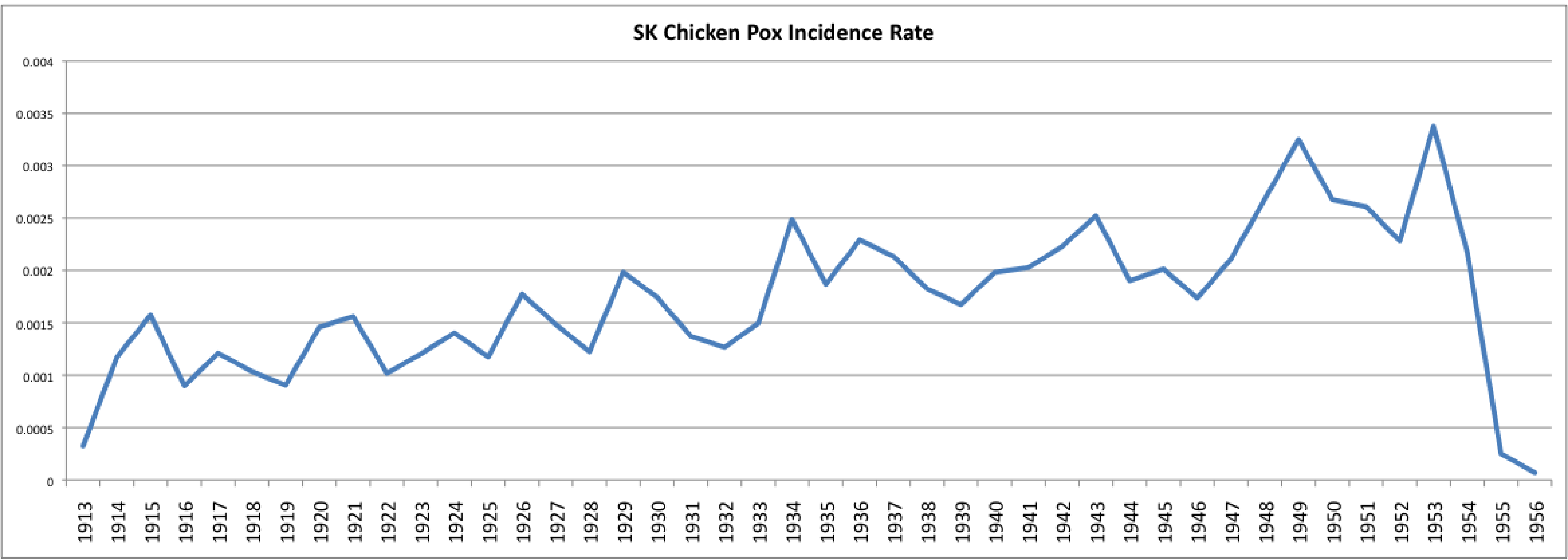

Chickenpox
600
500
400
300
200
100
0
Jan. 1942
Mar. 1942
May 1942
July 1942
Sept. 1942
Nov. 1942
Jan. 1943
Mar. 1943
May 1943
July 1943
Sept. 1943
Nov. 1943
Jan. 1944
Mar. 1944
May 1944
July 1944
Sept. 1944
Nov. 1944
Jan. 1945
Mar. 1945
May 1945
July 1945
Sept. 1945
Nov. 1945

Saskatchewan Childhood Diseases






SK Whooping Cough (Pertussis) Incidence Rate
0.0025
0.002
0.0015
0.001
0.0005
0
1910
1913
1916
1919
1922
1925
1928
1931
1934
1937
1940
1943
1946
1949
1952
1955
1958
1961
1964
1967
1970
1973
1976
1979
1982
1985
1988
1991
1994
1997
2000


SK Chicken Pox Incidence Rate
0.004
0.0035
0.003
0.0025
0.002
0.0015
0.001
0.0005
0
1913
1914
1915
1916
1917
1918
1919
1920
1921
1922
1923
1924
1925
1926
1927
1928
1929
1930
1931
1932
1933
1934
1935
1936
1937
1938
1939
1940
1941
1942
1943
1944
1945
1946
1947
1948
1949
1950
1951
1952
1953
1954
1955
1956

Slides Adapted from External Source

Redacted from Public PDF for Copyright Reasons

Nonlinearity (in state variables)

- Effect of multiple policies non-additive
- Doubling investment does not yield doubling of results
- Leads to
  - Multiple basins of tracking (equilibrium)

Multiple Equilibria & Tipping Points

- Separate basins of attraction have qualitatively different behaviour
  - Oscillations
  - Endemic equilibrium
  - Disease-free equilibrium

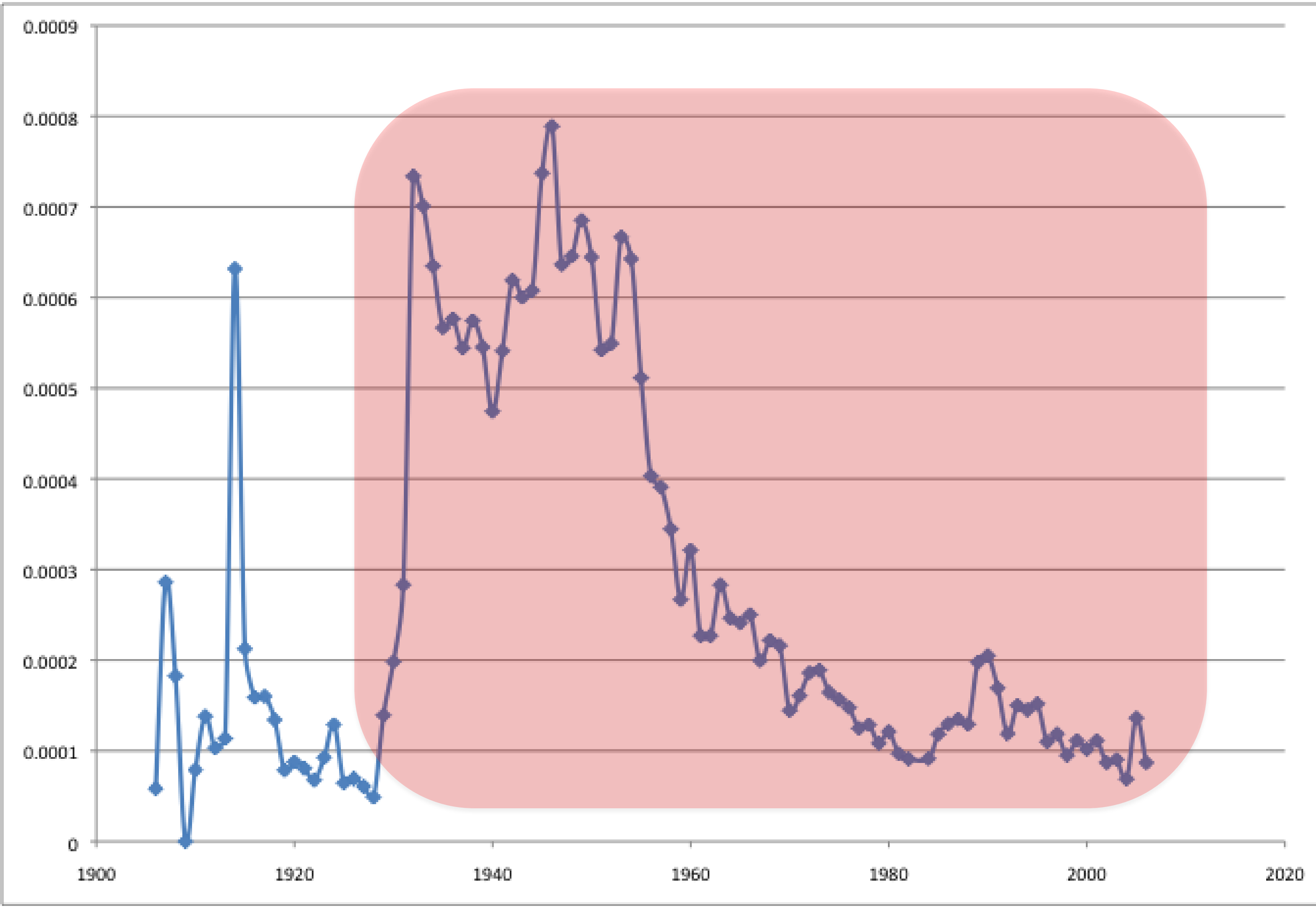
Equilibria

- Disease free
  - No infectives in population
  - Entire population is susceptible
- Endemic
  - Steady-state equilibrium produced by spread of illness
  - Assumption is often that children get exposed when young

Slides Adapted from External Source

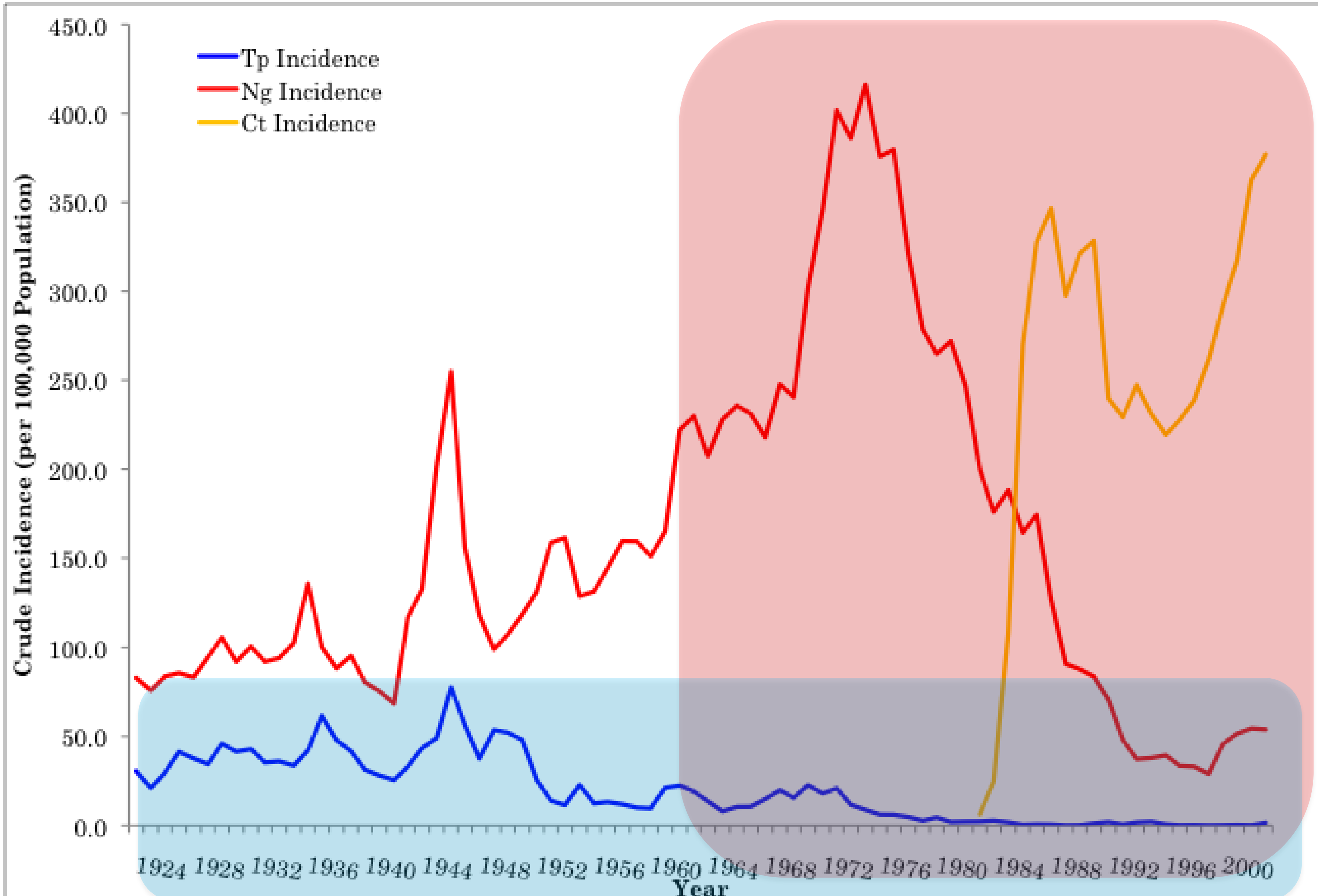
Redacted from Public PDF for Copyright Reasons

TB In SK

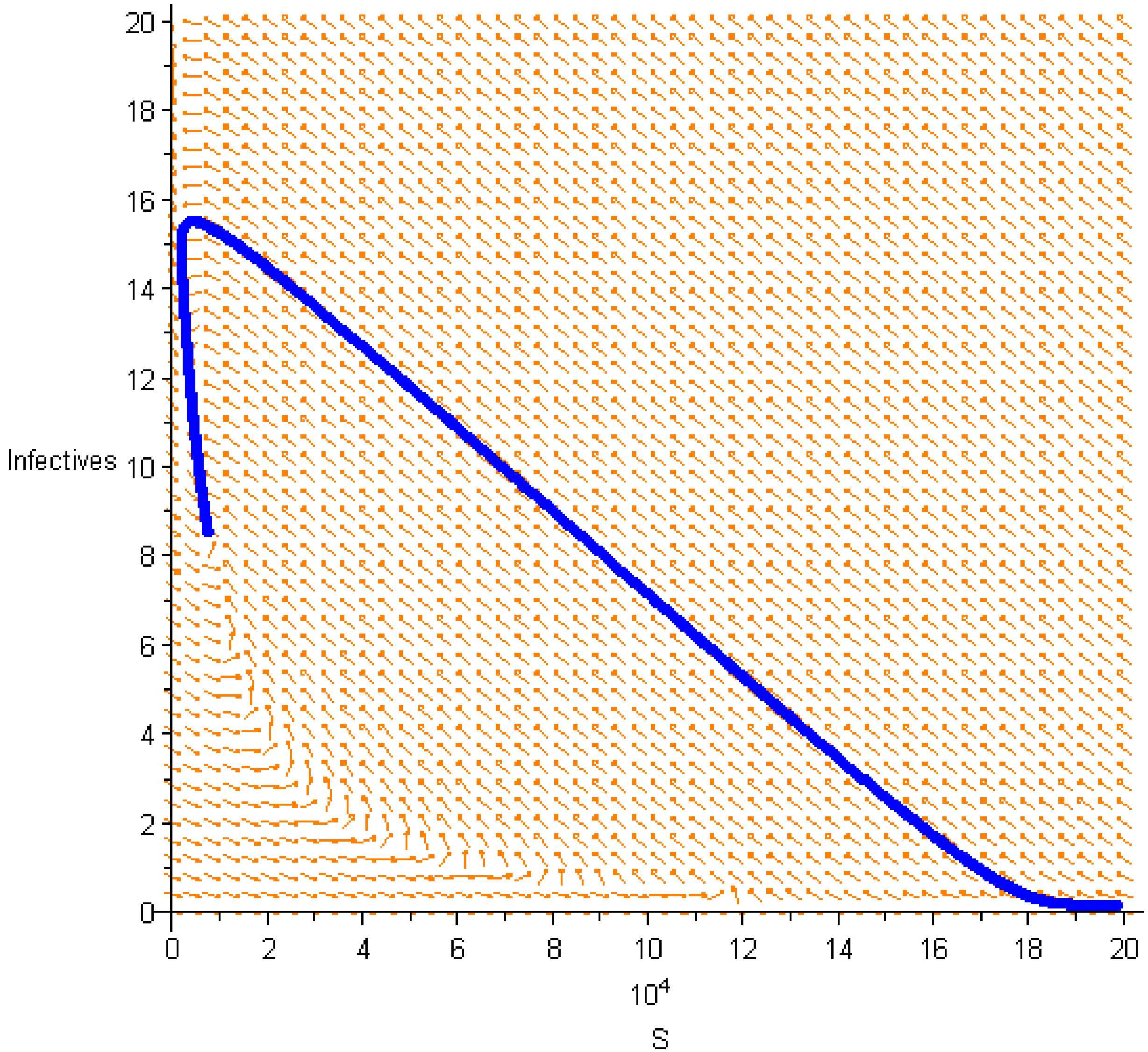


0.0009
0.0008
0.0007
0.0006
0.0005
0.0004
0.0003
0.0002
0.0001
0
1900
1920
1940
1960
1980
2000
2020

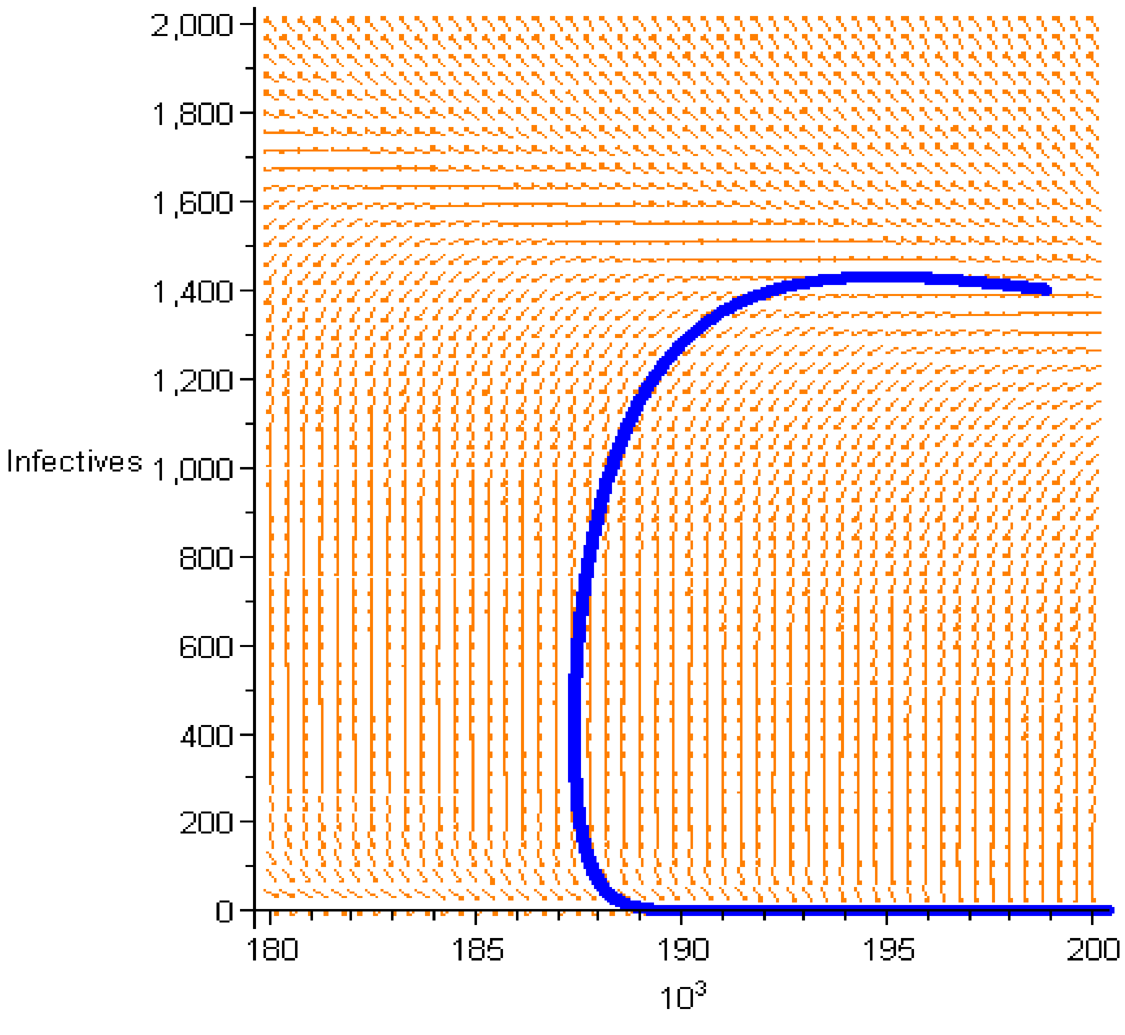
Example: STIs



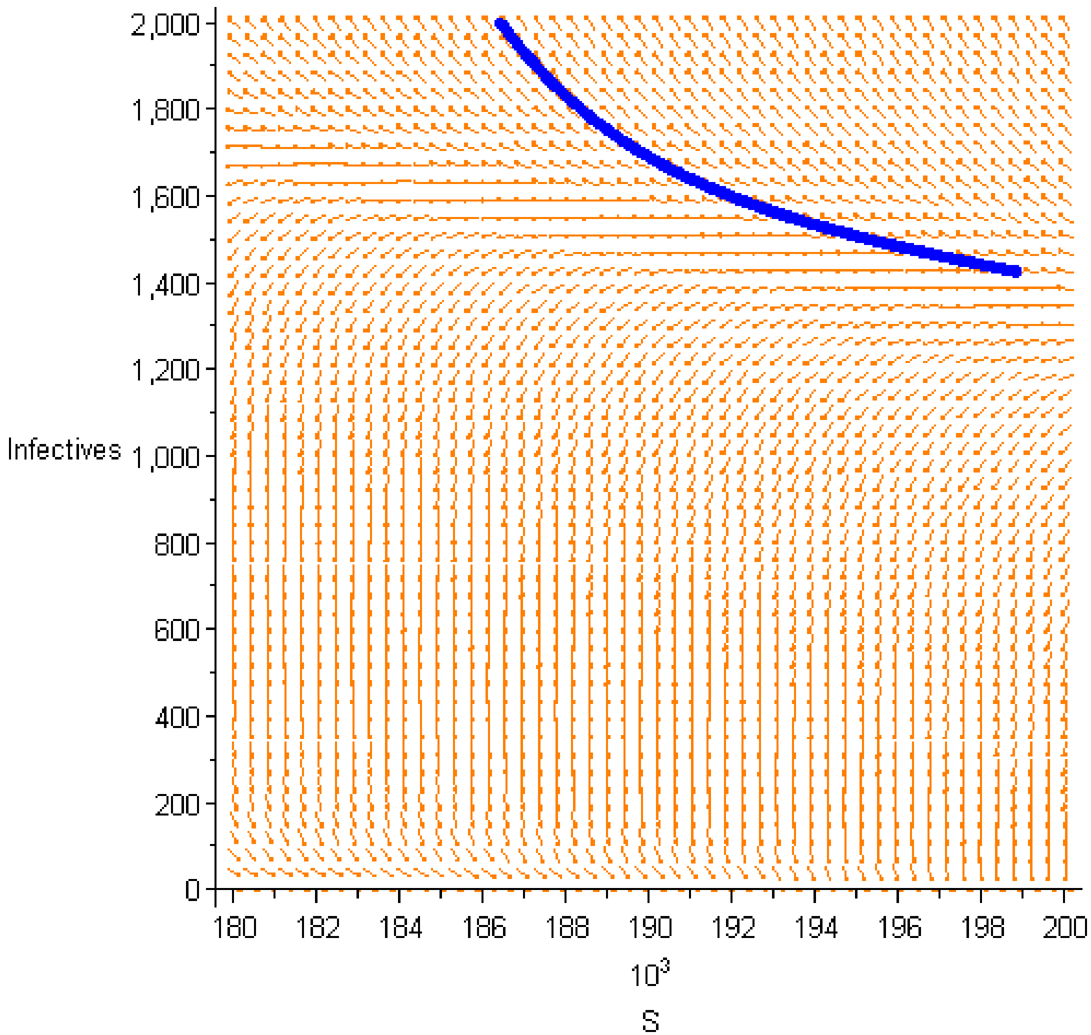
$R_0 < 1$: 200 HC Workers, I_0=1425



$R_0 < 1$: 200 HC Workers, I_0=1400

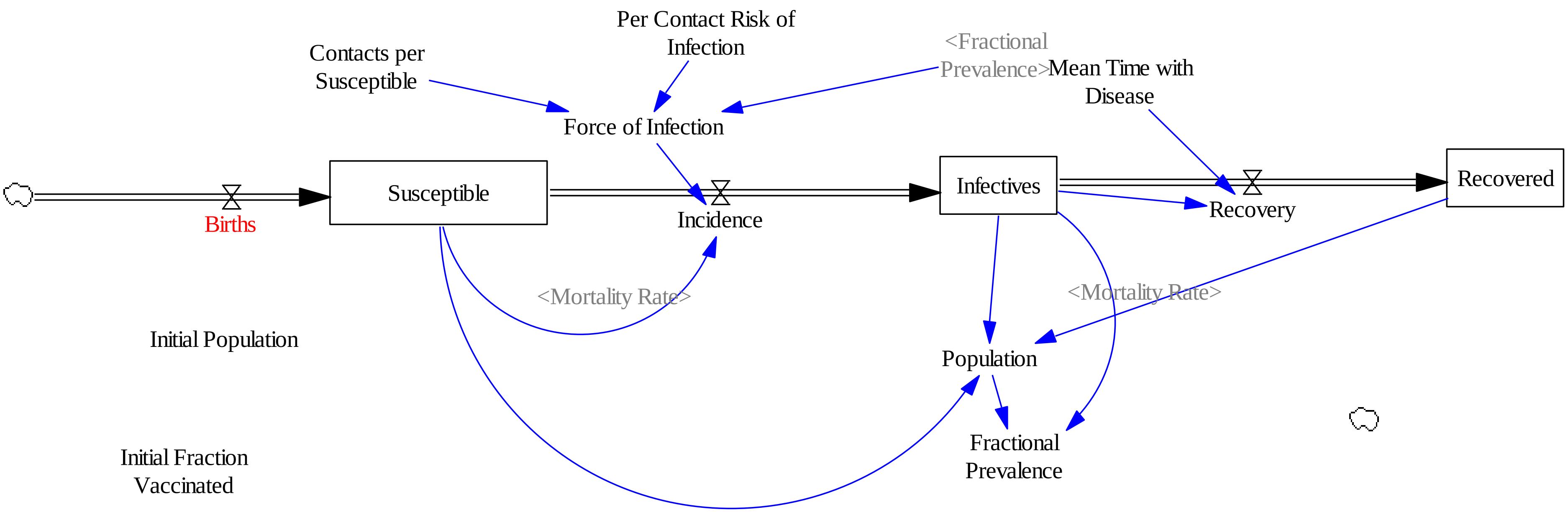


$R_0 < 1$: 200 HC Workers, I_0=1425



Kendrick-McKermack Model

- Partitioning the population into 3 broad categories:
  - Susceptible (S)
  - Infectious (I)
  - Removed (R)


Per Contact Risk of Infection
Contacts per Susceptible
<Fractional Prevalence>
Mean Time with Disease
Force of Infection
Births
Susceptible
Incidence
Infectives
Recovery
Recovered
<Mortality Rate>
<Mortality Rate>
Initial Population
Population
Initial Fraction Vaccinated
Fractional Prevalence

Shorthand for Key Quantities for Infectious Disease Models: Stocks

- *I* (or *Y*): Total number of infectives in population
  - This could be just one stock, or the sum of many stocks in the model (e.g. the sum of separate stocks for asymptomatic infectives and symptomatic infectives)
- N: Total size of population
  - This will typically be the sum of all the stocks of people
- S (or *X*): Number of susceptible individuals

Key Quantities for Infectious Disease Models: Parameters

- Contacts per susceptible per unit time: c
  - e.g. 20 contacts per month
  - This is the number of contacts a given susceptible will have with *anyone*

- Per-infective-with-susceptible-contact transmission probability: β
  - This is the per-contact likelihood that the pathogen will be transmitted from an infective to a susceptible with whom they come into a single contact.

Intuition Behind Common Terms

- I/N: The Fraction of population members (or, by assumption, contacts!) that are infective
  - Important: Simplest models assume that this is also the fraction of a given susceptible's contacts that are infective! Many sophisticated models relax this assumption
- c(I/N): Number of *infectives* that come into contact with a susceptible in a given unit time
- c(I/N)β: "Force of infection": *Likelihood a given susceptible will be infected per unit time*
  - The idea is that if a given susceptible comes into contact with c(I/N) infectives per unit time, and if each such contact gives β likelihood of transmission of infection, then that susceptible has roughly a total likelihood of c(I/N) β of getting infected per unit time (e.g. month)

Key Term: Flow Rate of New Infections

- This is the key form of the equation in many infectious disease models
- Total # of susceptiblesinfected per unit time

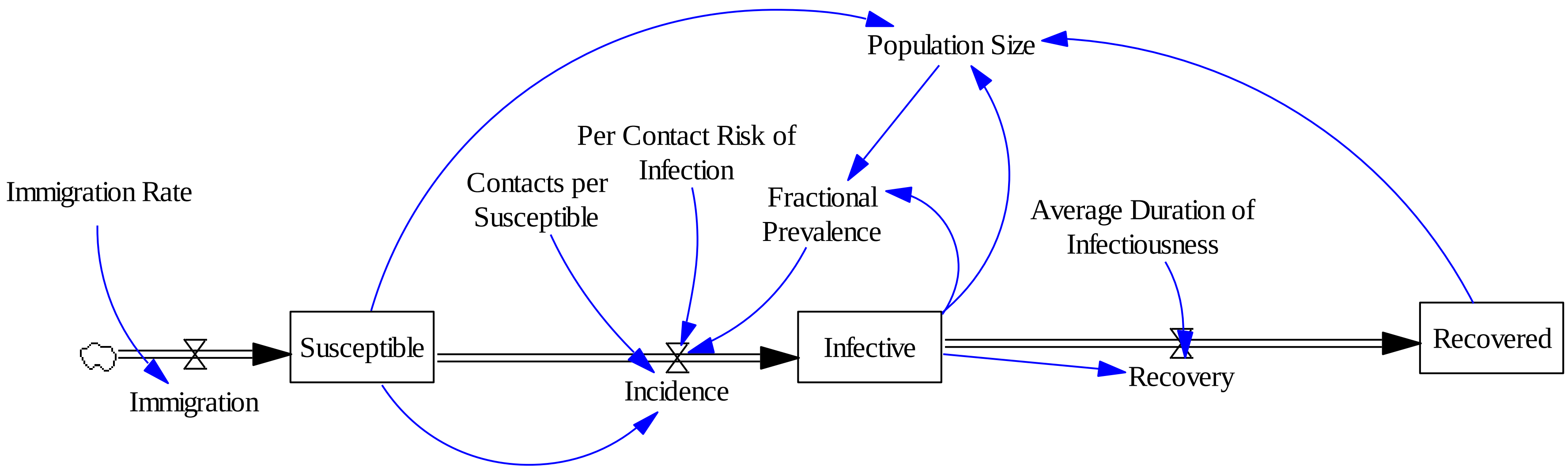
  # of Susceptibles * "Likelihood" a given susceptible will be infected per unit time = S*("*Force of Infection*") =S(c(I/N)β)

  - Note that this is a term that multiplies both S and I !
    - This is much different than the purely linear terms on which we have previously focused
  - "Likelihood" is actually a likelihood density (e.g. can be >1 – indicating that mean time to infection is <1)

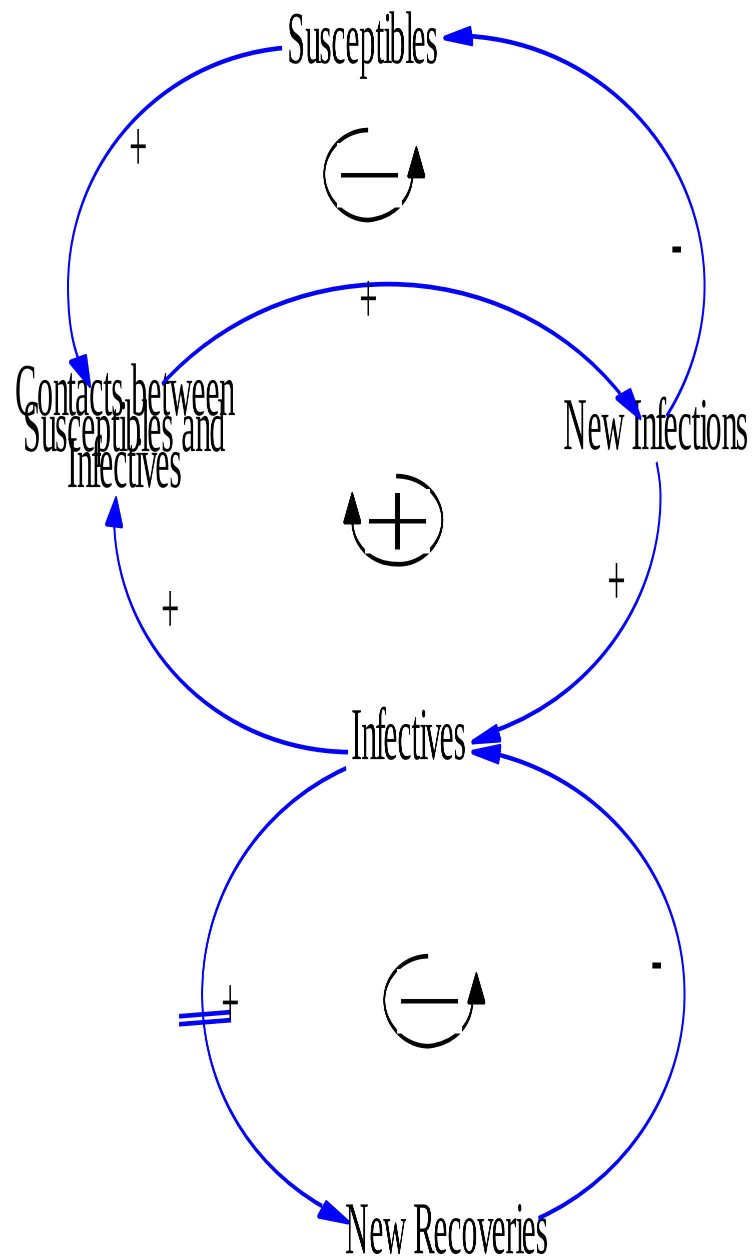
Another Useful View of this Flow

- Recall: Total # of susceptibles infected per unit time = # of Susceptibles * "Likelihood" a given susceptible will be infected per unit time = S*("*Force of Infection*") = $S(c(I/N)\beta)$
- The above can also be phrased as the following:$S(c(I/N)\beta)=I(c(S/N)\beta)$=# of Infectives * Average # susceptibles infected per unit time by each infective
- This implies that as # of susceptibles falls=># of susceptibles surrounding each infective falls=>the rate of new infections falls ("Less fuel for the fire" leads to a smaller burning rate

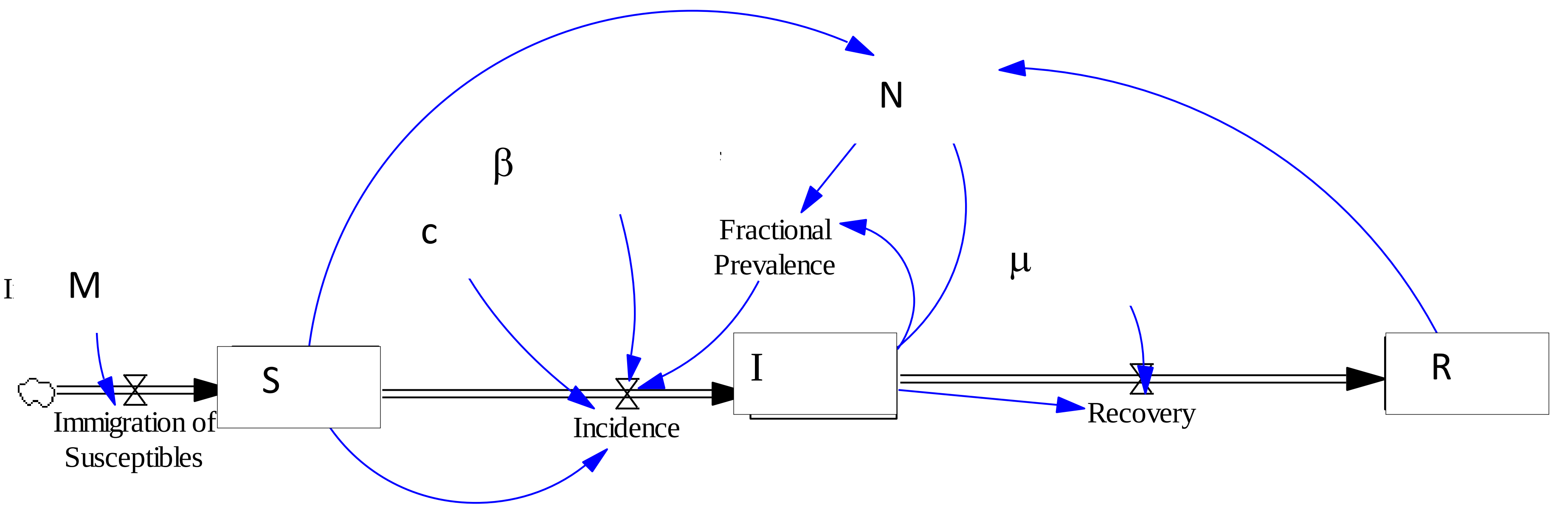
Basic Model Structure



Associated Feedbacks



Mathematical Notation

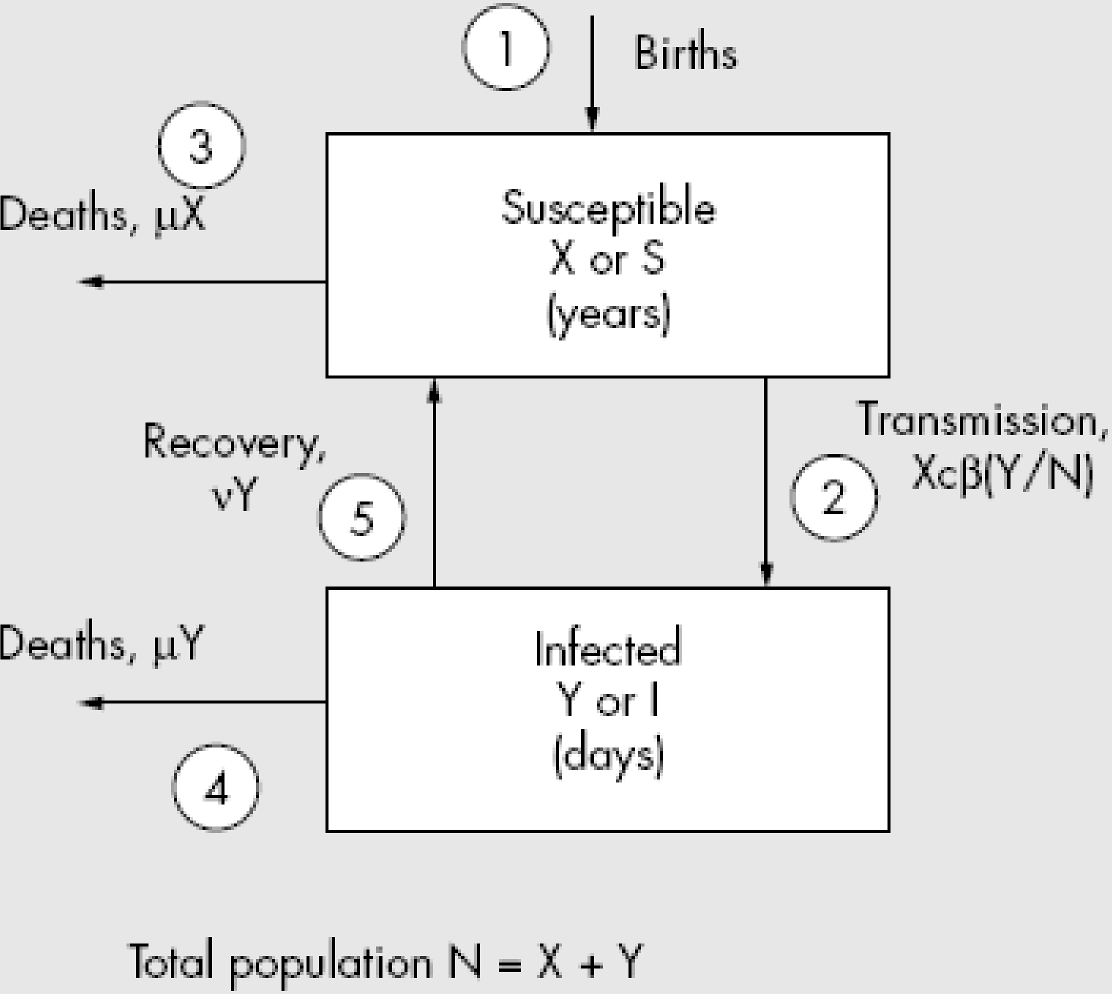


Underlying Equations

$$\dot{S} = M - c\left(\frac{I}{N}\right)\beta S$$

$$\dot{I} = c\left(\frac{I}{N}\right)\beta S - \frac{I}{\mu}$$

$$\dot{R} = \frac{I}{\mu}$$



in ① out ② out ③ in ⑤

$$\frac{dX}{dt} = +B - Xc\beta\,\frac{Y}{N} - \mu X - \nu Y$$

+

in ② out ④ out ⑤

$$\frac{dY}{dt} = +Xc\beta\,\frac{Y}{N} - \mu Y - \nu Y$$

$$\frac{dN}{dt} = +B - \mu X - \mu Y$$

Figure from Garnett, G. P. (2002). An introduction to mathematical models in sexually transmitted disease epidemiology. Sexually Transmitted Infections, 78(1), 7-12.